Usage of and attitudes about green tea extract and Epigallocathechin-3-gallate (EGCG) as a therapy in individuals with Down syndrome

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Abstract

Objective: Usage of and views concerning alternative therapies in the DS community are not well documented. Some positive effects of green tea extracts (GTE) containing Epigallocathechin-3-gallate (EGCG) have been reported in individuals with DS and DS mouse models, but minimal improvements or detrimental effects of pure EGCG treatment have been reported in DS mouse models. Given the uncertainty about the effectiveness of these supplements, the goal of this study was to determine the relative prevalence of and attitudes about GTE/EGCG treatments among DS caregivers.

Methods: An anonymous survey about attitudes and usage of GTE/EGCG in individuals with DS was completed by caregivers of these individuals.

Results: GTE/EGCG treatment was provided by 18% of responding caregivers who were mostly younger, highly educated, and utilized scientific sources and other parents to influence their decision to use GTE/EGCG. Individuals with DS who received GTE/EGCG were characterized as less severely disabled. Most caregivers who did not give GTE/EGCG reported concerns about potential side effects and lack of effectiveness. Few caregivers consulted with medical providers about GTE/EGCG usage.

Conclusions: These results demonstrate a need for communication between caregivers, medical providers, and scientists about potential benefits and risks for adverse effects of GTE, EGCG, and other nutritional supplements in individuals with DS.

1. Introduction

Trisomy of human chromosome 21 (Hsa21), affecting approximately 1/800 live births (1), results in Down syndrome (DS) and alters cognitive, skeletal, and cardiac functions. Individuals with DS have lower intelligence quotients (IQ), though wide ranges of IQs are reported (2). Cognitive traits in individuals with DS have been refractory to conventional therapeutics and may worsen with age, often leading those caring for individuals with DS to consider alternative treatments including nutritional supplements (3-6).

Increasing numbers of conventional and alternative therapies have been proposed, tested in preclinical DS mouse models, and progressed to clinical trials in individuals with DS (7). Some of these therapies have targeted specific neurotransmitter systems or aberrant neural pathways, based on their contribution to cognitive and behavioral phenotypes. Additional treatments have targeted genetic or molecular mechanisms thought to be altered by Ts21 (6, 7).

DYRK1A (Dual specificity tyrosine phosphorylation-regulated kinase 1A), a gene located on Hsa21, is a serine threonine kinase enzyme that appears to have a critical role during brain development, and three copies of DYRK1A has been hypothesized to lead to cognitive and skeletal deficits associated with Ts21 (8). Subtraction of one copy of *Dyrk1a* in otherwise trisomic DS mouse models improved cognitive, neurological, and skeletal deficits (9-12). Thus, trisomic DYRK1A has been recognized as a rational target for therapeutic drug treatments (8, 13).

Epigallocatechin gallate (EGCG) is a putative treatment for DS phenotypes due to its ability to reduce DYRK1A activity in vitro (14), and reduce oxidative stress and mitochondrial energy deficits (6). EGCG is the major polyphenol (50-75%) found in green tea extracts (GTE) and is a candidate treatment to improve cognitive and developmental phenotypes associated with

DS. Treatment of mice with an extra copy of *Dyrk1a* with GTE improved performance on a task of learning and memory and improved neurological abnormalities (15-17). Administration of GTE containing EGCG in the Ts65Dn DS mouse model improved hippocampal dependent learning (18). [For a comprehensive review of these treatments see (19)]. These preclinical data in mice suggest that treatment with GTE with EGCG could correct some neurological deficits and improve hippocampal-dependent learning and memory in trisomic mice.

Other studies have failed to confirm positive effects of EGCG in normalizing DS phenotypes, particularly preclinical experiments using pure EGCG treatment and assessing DS-related neurological and skeletal deficits. Treatment of Ts65Dn mice with ~9 mg/kg/day EGCG improved several bone deficits, and some improvements were similar to those found in Ts65Dn mice with only two copies of *Dyrk1a* (12). A dosage of ~9 or 20mg/kg/day EGCG, however, did not improve cognitive defects in Ts65Dn mice (20). GTE supplements containing EGCG were detrimental to bone strength in Ts65Dn mice (21). Treatment with 50 mg/kg/day EGCG also did not improve DS-related cognitive deficits and worsened skeletal phenotypes in Ts65Dn mice (22).

A phase-one type trial in 31 individuals with DS given GTE with ~9 mg/kg/day EGCG for 3 months found that individuals with DS receiving GTE showed improvement in memory and executive function (18). In a second trial, 84 individuals with DS received GTE with 8-12 mg/kg/day EGCG or placebo for 12 months while participating in additional cognitive training. Individuals who received GTE exhibited some improvements in visual recognition, executive function, and adaptive behavior (23). We hypothesized that these reports of modest improvements in individuals with DS after treatment with GTE would spur therapeutic usage of GTE and EGCG supplements.

In a survey examining the use of dietary supplements in individuals with DS, approximately half of the individuals with DS were receiving at least one supplement and 8.7% indicated that they used GTE (3). Because of published reports of positive, null, and negative effects in preclinical studies of GTE and EGCG, and trials examining the effects of GTE in individuals with DS, we wanted to characterize the DS community's knowledge, perception, and experience with GTE and quantify the administration of GTE/EGCG in individuals with DS.

2. Materials and methods

A Qualtrics-based survey, "Attitudes about and usage of Epigallocatechin-3-gallate (EGCG) as a therapy in individuals with Down syndrome" was designed by authors JRW, RJR, CMD, RL and CRG, reviewed and modified to include suggestions by a DS-Connect (https://dsconnect.nih.gov/) review panel, and given exempt status by the Indiana University Institutional Review Board as protocol number 1710755582. The survey was disseminated via DS-Connect and through various DS clinics and associations across the United States via an email to prospective respondents. The email described the survey and the eligibility criteria as a parent or caregiver of an individual with DS and asked them to complete the survey. The survey remained open for a 6-month period from January-June 2018.

Based on their response to the first question, "Have you ever used EGCG or green tea extract to treat your child?", participants were divided into separate tracks. According to their answer to the first question, caregivers were asked questions assessing their attitudes toward and extent of GTE/EGCG usage. Individuals from all tracks were asked demographic questions about the individual with DS and the caregiver, education levels of the individual with DS and the caregiver, therapy, medication, and perceived level of intellectual ability. Caregivers who had knowledge of GTE/EGCG were asked about how they learned about the supplement and their interactions with other individuals with DS. Those who had or were giving GTE/EGCG were asked questions about the kind of supplement used, supplement administration, and expectations for improvement.

This study utilized a cross-sectional design with a single time point, during which participants completed our survey. Descriptive statistics (e.g., frequencies, means, and standard deviations) were used to analyze the responses in order to capture the distribution of responses

for each question. A one-way analysis of variance (ANOVA), which tests whether a continuous dependent variable (e.g., age) varies between conditions, was performed to examine whether the age of caregivers significantly differed across GTE/EGCG usage groups. Finally, Chi-Square tests of independence were performed to test whether there were significant relationships between categorical variables. In particular, we examined relationships between: caregiver education level and learning about GTE/EGCG from other caregivers, classroom environment of individual with DS and GTE/EGCG usage, and child's level of intellectual disability and GTE/EGCG usage.

3. Results

3.1 Demographic Information of the Entire Sample (N=348)

A total of 348 caregivers of individuals with DS responded to the survey and answered the first question "Have you ever used EGCG or green tea extract to treat your child?" in one of four ways: A. Yes, I currently give EGCG to my child (*N*=47, 13.5%); B. Yes, but I stopped giving EGCG to my child (*N*=17, 4.9%); C. No, I have never given EGCG to my child, but I am aware of its use (*N*=71, 20.4%); or D. I don't know anything about EGCG and I have never given it to my child (*N*=213, 61.2%). Of all respondents, 18.4% reported giving GTE or EGCG to their dependent with DS currently or in the past. Demographics of caregivers are found in Table 1. The average age of the caregivers was significantly different among GTE/EGCG usage groups, $F(3, 315)=11.255$, $p<0.001$. Caregivers who reported not knowing about and not giving GTE/EGCG to their child were significantly older than those who reported they were aware of its use but had never given it to their child ($p<0.001$, $d=0.66$, *Mean Difference*=6.54, *SE*=1.47, 95% CI [2.74, 10.34]), and those who reported currently giving GTE/EGCG to their child, ($p<0.001$, $d=0.81$, *Mean Difference*=7.64, *SE*=1.79, 95% CI [3.01, 12.26]). A significant relationship was observed between caregiver education and learning about GTE/EGCG from other caregivers; the higher the education level of the caregiver, the less likely they were to hear about GTE or EGCG usage from other caregivers [$\chi^2(4, N=115)=10.32$, $p=0.035$].

The characteristics of individuals with DS as provided by their caregivers are found in Table 2. There was a significant relationship between classroom environment of the individual with DS and use of GTE/EGCG, [$\chi^2(6, N=112)=14.04$, $p=0.029$]; individuals with DS who were given GTE or EGCG were more likely to be in a mainstreamed classroom. There was also a non-significant trend in the relationship between the child's level of intellectual disability and GTE or

EGCG usage, [$\chi^2(4, N=113)=8.39, p=0.078$]; individuals with DS who received GTE or EGCG were reported as having a milder disability than individuals with DS with a caretaker who responded that they did not know about GTE/EGCG.

3.2 Current GTE/EGCG Users

At the time the survey was given, 47 of the respondents reported administering GTE or EGCG to their child with DS. For these responses, the average age of these caregivers was 44.1 (*SD*=7.7) years, and the child's average age was 8.3 (*SD*=7.1) years (*range*: 8 months-28 years). The mean reported weight of the child was 27.4 kgs (*SD*=18.1), and the mean reported mg/day of EGCG given to the individual was 272 mg/day (*SD*=314.1; *range*: 0-1200mg). Of the respondents who reported both weight and mg/day, the mean dosage was 10 mg/kg/day EGCG.

Respondents who currently administer GTE or EGCG heard about this nutritional supplement mostly through scientific publications (Fig. 1A). The majority (28/40) administered GTE/EGCG once a day, 9/40 twice a day, two people less frequently than every other day, and one person every other day. The majority (36/40) purchased the supplement online, and two respondents each reported buying in a supplement shop or a supermarket. The most common form of GTE or EGCG was capsule (22/40) followed by powder (17/40), and two reported using liquid (individuals chose multiple options in their response). Three people changed forms of the nutritional supplement during treatment. Information about brand usage is found in Supplemental Table 1.

For individuals receiving GTE or EGCG at the time of the survey, the mean age that treatment began was 6.5 years (*range*: 0 months-27 years). Twenty-three people had been using GTE/EGCG for more than 1 year, 12 individuals between 6 months-1 year, 4 between 1 month-6 months, and one person reported giving GTE/EGCG for less than a month. Three caregivers

perceived benefits from treatment within a few months, 8 within a month, 7 in ~2 weeks, while others reported seeing benefits as soon as a week (*N*=7) or a few days (*N*=3) (Fig. 1B). Many individuals reported that their expectations were met or somewhat met while giving GTE/EGCG (Fig. 1C) including improvements in cognition, learning, memory, DYRK1A and GABA inhibition, increased energy, and speech. Only one person reported a side effect that the supplement interfered with sleep.

3.3 Previous users of GTE or EGCG

Of the 17 individuals who used GTE/EGCG in the past, the mean age of the caregiver was 45.1 (*SD*=8.6) years, and the child's mean age was 10.5 (*SD*=6.9) years (*range*: 3 years-26 years). The child's average weight during the time of administration was 27.4 kg (*SD*=21.9) and the self-reported dosage was 385.3 mg/day (*SD*=632.4; *range*: 1-2,000 mg/day). Of the respondents who gave both weight and dosage, 28 mg/kg/day EGCG was the average dose. The top responses for where they heard about GTE/EGCG were scientific studies, other parents and the internet (Fig. 2A).

The mean age at treatment of individuals with DS who received GTE or EGCG and subsequently stopped was 10.5 years (*range*: 6 months-22 years). The majority (11/12) administered GTE/EGCG once a day, with the most common form being powder (7/14), followed by capsule (6/14) and liquid (1/14). No one reported changing forms during the time of administration. Most reported using between 1-6 months (*N*=5) or only trying it once (*N*=4). Fewer reported using it for 6 months to a year (*N*=2) or less than a month (*N*=2). Only one person reported using for more than a year before stopping. Supplemental Table 1 contains the most commonly reported GTE or EGCG brands used for prior and current users.

Ten individuals reported seeing no benefits in individuals with DS for whom they cared. Two people reported seeing improvement in verbal communication, and one was unsure if they saw improvement. Caregivers stopped giving GTE/EGCG because they saw no improvement (*N*=4), their child did not like the supplement (*N*=4), the child had an adverse reaction (*N*=2), or the supplement was too expensive (*N*=2). One person reported finding a better supplement. Three people from the "other" category reported the following reasons: their child's physician did not recommend usage, wanting to limit the number of supplements the child received, and forgetting to reorder.

Six of ten people reported no side effects, and the other four reported side effects such as "over exertion, subsequent fatigue", "turn pale, seemed out of it", "lethargy", and "possible increase in aggression". Eight people reported that their expectations were not met, one person reported their expectations were somewhat met, and one reported their expectations were met.

Caregivers aware of EGCG but have never used it

The average age of the caregiver in the group who heard of GTE or EGCG but not used it was 45.2 (*SD*=8.9) years, and the child's average age was 10.75 years (*SD*=9.5, *range*: 2 years-48 years). In this group, most caregivers heard about GTE/EGCG from the internet (Fig. 2B). Potential side effects and lack of evidence for effectiveness were leading reasons for why caregivers chose not to administer GTE or EGCG (Fig. 2C). Other reasons for not using GTE/EGCG aggregated within the following five themes: considering it, uncertain of proper dosage/administration, cost, lacking knowledge, and concern over child's health/potential interactions.

3.4 Caregivers who didn't know anything about EGCG

The average age of the 214 caregivers who knew nothing about EGCG was 51.8 (*SD*=10.9) years, and the average age of the individual with DS from this group was 18 years (*SD*=11.8, range: 1 year-62 years).

4. Discussion

The present study found 13.5% of the respondents currently, and 4.9% previously gave GTE/EGCG to individuals with DS. A recent study of dietary supplement use in individuals with DS reported 8.7% of respondents used GTE or EGCG (3). Differences between the two studies in the number of reported users of GTE and EGCG may be due to differences in sample sizes between the two studies; alternatively, the current study may have attracted more individuals who are using GTE/EGCG because of the specific mention of these supplements in the title of the survey. Because of the reports of trials with GTE/EGCG in individuals with DS, some respondents of the previous study (3) may not have considered EGCG a dietary supplement, but rather a verified treatment. In agreement with the previous study where parents learned about all supplements through a parent group or friend, many caregivers who currently or formerly administered GTE or EGCG in the present study reported learning about GTE/EGCG through a parent group or friend. Yet, of those currently or formerly using GTE or EGCG, many caregivers in this study identified as highly educated and reported reading scientific literature in addition to learning about GTE/EGCG from other parents. Current users were the only group to respond "no" more often than "yes" when asked if their child was taking any additional medications. Reported side effects, lack of improvement, and cost were among the main reasons for discontinuation of GTE/EGCG treatment.

Treatment with green tea and EGCG has been linked to hepatotoxicity that likely depends on dosage, route of administration, and EGCG or other catechin content (24). Adverse effects were observed when high concentrations of GTE or EGCG were taken in a single dose, but fewer adverse effects when taken as a beverage (24, 25). Safe levels of EGCG in humans have been determined to be around 300 mg/day (24-26). Dosages from 150-800 mg/kg EGCG have

been linked to damage in the liver, kidney, thymus, spleen, and pancreas of EGCG in adults (24, 25, 27). There is a high risk of hepatoxic interactions between dietary supplements and other drugs, and most individuals are unaware of such interactions (28).

The results from this study found a wide range in EGCG dosage with a mean of 351 mg/day and a range up to 2000 mg/day. A dosage of 300 mg/day or greater was reported by 14/64 respondents who have used or are currently using EGCG. In comparison, the small human studies administered GTE with 9 mg/kg/day EGCG for 3 months to individuals from 14-19 years of age (18) and 8-12 mg/kg/day for 12 months to individuals from 16-34 years (23).

Many respondents also reported that individuals with DS were taking additional medications that could interact with GTE/EGCG. Animal studies indicate that GTE/EGCG could increase the bioavailability of diltazem, verapamil, tamoxifen, simvastatin, 5-fluorouracil, and nicardipine and decrease bioavailability of quetiapine, sunitinib, clozapine, and nadolol (29). In humans, GTE was shown to interact with simvastatin, rosuvastatin, sildenafil, tacrolimus, warfarin and nadolol, depending on GTE dosage and human variability (30, 31). Also in humans, large amounts of GTE/EGCG may interfere with drugs like rosuvastatin that are substrates of organic anion transporting polypeptides (OATP), but this may also may differ according to treatment regimen and allelic differences in the OATP genes (29, 30). Some of the GTE/EGCG-drug interactions may contribute to liver damage (29). One individual in the group who heard of GTE or EGCG but not used it reported using sildenafil. Caution should be exercised with individuals taking medications with supplemental GTE/EGCG. The age of the individuals and duration of the treatment in our survey varied from 0-27 years (M=6.5 years) and most individuals received GTE/EGCG for over a year. The majority of individuals who responded to our survey gave GTE/EGCG to individuals who were >10 years of age (57%) and 53% began

giving the supplement to individuals with DS between 1-10 years of age, with an additional 19% of individuals with DS receiving the supplement at less than a year of age. Forty-one percent of the caregivers who gave GTE/EGCG but had discontinued gave it to individuals with DS under the age of 10, and 29% of people who had discontinued administration of GTE/EGCG gave it to individuals with DS less than 12 months of age. No studies of GTE/EGCG have been done on humans less than 14 years of age, raising concerns about administration of GTE/EGCG to young individuals with DS without knowing any potential dangers of GTE/EGCG at a young age.

There were also widely ranging amounts of EGCG in GTE utilized (Supplemental Table 1). Only five individuals with DS who were currently receiving or had received GTE/EGCG used the brand (Life Extensions) used in the small treatment trials (18, 23). Because the contents of supplements are not highly regulated, each supplement may not contain the advertised amount of EGCG (21). Additionally, the content and number of other polyphenols found in different supplements may affect the bioavailability of EGCG (17, 32). Both of these factors may affect the therapeutic potential of the GTE. Because studies that have reported effectiveness of EGCG were administered as part of a GTE, other components of the GTE besides EGCG may provide the reported positive effect on phenotypes (19). While EGCG is often touted as the treatment to correct phenotypes associated with DS, studies examining EGCG alone have only been done in DS model mice. The separate effects of EGCG or other catechins found in GTE have not been tested in humans with DS.

Besides phenotypes associated with DS, GTE/EGCG has been examined for effectiveness in other disorders including weight loss, eyestrain and blood pressure, prostate cancer, breast cancer, and cardiovascular disease (33-37). In most of these studies, there were treatment and control groups with particular designated outcomes. A survey of unaffected

brothers of men with prostate cancer found that approximately one-third of the unaffected men were using a vitamin or supplement marketed for prevention of prostate cancer (33). About 6% of the men had used green tea, with ~5% currently using. Though not statistically significant, higher educational attainment and higher household income was associated with the use of prostrate related vitamins and supplements. Most individuals were using 2-3 supplements and 23% received information about the supplement from a family member, 24% from a book or article, and 15% each from a physician other than an urologist or the internet or news report. Similar to our study, individuals were using supplements for a disorder based on information from articles or the internet and had a high educational attainment. Another survey study that examined complimentary medicine usage in cancer treatment found that 35% of individuals were using green tea (38). Eighty-six percent of their oncologists did not ask whether they were using complimentary medicines. Like our study, those that used complimentary medicine were significantly younger than those that did not and most did not consult with their health care provider. There were a number of potential significant interactions between anticancer agents and green tea.

EGCG is just one of the supplements proposed to correct deficits in individuals with DS. Other supplements that are commonly given to individuals with DS include Nutrivene, antioxidants, vitamins, and fats/fatty acids; the average child with DS receives a range of 1-18 supplements with an average of 3.3 per child (3). Interaction of these supplements with GTE/EGCG is not currently known, but given the drug-GTE/EGCG interactions, the potential for adverse results exists. The underreporting of supplement use to clinicians may exacerbate the risk of adverse interactions of GTE/EGCG and drugs or other supplements (31).

5. Limitations

Limitations of this study include that the results were self-reported. These data may be biased by individuals who answered our study because they knew about or were using GTE or EGCG. However, ~60% of the individuals who responded to the survey reported not using GTE/EGCG. In addition, many individuals did not fully respond to all of the questions, and some reported brands of GTE without specifying the product name. Those who responded to the survey were likely connected to other caregivers of individuals with DS because the study was disseminated through DS-Connect and DS organizations. Individuals who were associated with DS-Connect were likely very interested in research, and that may have influenced the education status of the caregiver or the literature about GTE/EGCG they were able to access. The sample sizes for each group were largely uneven; prior users made up only ~5% of the responses.

6. Conclusion

A large majority of those who were aware of GTE/EGCG and had never used it indicated that they had found no evidence for the effectiveness or were concerned about potential side effects of GTE/EGCG. The majority of these individuals reported that they were familiar with EGCG through the internet. It may be that these individuals were aware of the positive and negative scientific studies about GTE/EGCG related to DS and elected not to administer the nutritional supplement for this reason. Relatively few of the caregivers who administered EGCG or had heard about it consulted a medical professional about its use. The DS community may benefit from further research regarding the efficacy and safety of GTE/EGCG, and discussing administration of this and all nutritional supplements with their medical providers.

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Disclosure Statement

The authors declare no conflicts of interest.

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Figure 1. Reports from caregivers currently giving EGCG to individuals with DS. (A) Descriptions of how caregivers learned about GTE/EGCG usage. (B) Reports of observed benefits of EGCG. “Other” responses included improvements in speech, energy, ability to focus, and “I don’t know”. (C) Description of level of satisfaction with the results observed after administering GTE/EGCG. *N*=40 in A and B, some caregivers provided multiple responses.

Figure 2. Reports from caregivers who have previously used EGCG or were aware of EGCG but never used it. (A) Reports of how caregivers that previously administered EGCG found out about it. *N*=14, many respondents chose multiple sources. (B) Descriptions of how caregivers that were aware of EGCG, but never gave it to the individual with DS found out about EGCG. *N*=67, many respondents chose multiple sources. (C) Reasons for not using EGCG from caregivers that knew about EGCG but never gave it to an individual with DS. *N*=71, many caregivers gave multiple responses.

Table 1: Demographics of caregiver respondents (*N*=348)

Caregiver Demographic Information									
Variables		I don't know anything about EGCG *N*=213		Never used EGCG but aware of use *N*=71		I have used EGCG in the past *N*=17		I currently use EGCG *N*=47	
		N	%	*N*	%	*N*	%	*N*	%
Highest level of education	High School Diploma or GED equivalent	6	2.9	1	1.4	0	-	1	2.1
	Some college	28	13.1	6	8.5	1	5.9	3	6.4
	Bachelor's degree	78	36.6	25	35.2	3	17.6	11	23.4
	Some graduate school	12	5.6	6	8.5	2	11.8	5	10.6
	Graduate degree	83	39	28	39.4	5	29.4	18	38.3
	No answer	6	2.8	5	7	6	35.3	9	19.1
Age (years)	18-30	0	-	0	-	0	-	2	4.3
	31-40	27	12.7	22	31	3	17.6	9	19.1
	41-50	72	33.8	26	36.6	6	35.3	20	42.6
	51-60	66	31	9	12.7	0	-	6	12.8
	61-70	32	15	4	5.6	1	5.9	1	2.1
	71-80	9	4.2	1	1.4	0	-	0	-
	No answer	7	3.3	9	12.7	7	41.2	9	19.1
Interact with other DS families *only 3 tracks included	Yes	-	-	66	93	12	70.6	38	80.9
	No	-	-	1	1.4	2	11.8	2	4.3
	No answer	-	-	4	5.6	3	17.6	7	14.9
Involved in support group *only 3 tracks included	Yes	-	-	59	83.1	12	70.6	35	74.5
	No	-	-	8	11.3	2	11.8	5	10.6
	No answer	-	-	4	5.6	3	17.6	7	14.9
Gender	Female	184	86.4	59	83.1	10	58.8	38	80.9
	Male	21	9.9	6	8.5	1	5.9	7	14.9
	Prefer not to identify	2	0.9	1	1.5	0	-	0	-
	No answer	6	2.8	5	7	6	35.3	2	4.3
Ethnicity	White or Caucasian	186	87.3	57	80.3	10	58.8	29	61.7
	Hispanic or Latino	8	3.8	4	5.6	0	-	4	8.5
	Black or African American	2	0.9	1	1.4	0	-	2	4.3
	Native American or American Indian	3	1.4	1	1.4	0	-	0	-
	Asian or Pacific Islander	5	2.3	1	1.4	1	5.9	1	2.1
	Other	2	0.9	2	2.8	0	-	2	4.3
	No answer	8	3.8	5	7	6	35.3	9	19.1
Estimated yearly household income	Less than $25,000	2	0.9	1	1.4	0	-	3	6.4
	$25,000- $50,000	16	7.5	2	2.8	0	-	3	6.4
	$50,000-$75,000	17	8	7	9.9	2	11.8	4	8.5
	$75,000-$100,000	34	16	12	16.9	2	11.8	3	6.4
	$100,000-$125,000	34	16	9	12.7	1	5.9	2	4.3
	More than $125,000	75	35.2	24	33.8	4	23.5	16	34
	Prefer not to identify	29	13.6	9	12.7	2	11.8	7	14.9
	No answer	6	2.8	7	9.9	6	35.3	9	19.1
Country currently residing in	In United States	201	94.4	64	90.1	11	64.7	25	53.2
	Outside of United States	1	0.5	2	2.8	0	-	9	19.1
	No answer	11	5.2	5	7	6	35.3	13	27.7

Table 2: Demographics of individuals with DS from those that responded to the survey (*N*=348)

Individual with DS Demographic Information									
Variables		I don't know anything about EGCG *N*=213		Never used EGCG but aware of use *N*=71		Used EGCG in the past *N*=17		Currently use EGCG *N*=47	
		N	%	*N*	%	*N*	%	*N*	%
Type of Down syndrome	Trisomy 21	199	93.4	65	91.5	12	70.6	34	72.3
	Mosaic	4	1.9	0	-	0	-	1	2.1
	Translocation	4	1.9	1	1.4	0	-	1	2.1
	No answer	6	2.8	5	7	5	29.4	11	23.4
Ethnicity	White or Caucasian	181	85	56	78.9	10	58.8	28	59.6
	Hispanic or Latino	10	4.7	4	5.6	0	-	5	10.6
	Black or African American	3	1.4	1	1.4	0	-	2	4.3
	Native American or American Indian	1	0.5	1	1.4	0	-	0	-
	Asian or Pacific Islander	4	1.9	1	1.4	2	11.8	1	2.1
	Other	11	5.2	3	4.2	0	-	2	4.3
	No answer	3	1.4	5	7	5	29.4	9	19.1
Educational environment	Mainstreamed classroom or inclusive	64	30	41	57.7	3	17.6	15	31.9
	Special education center	39	18.3	4	5.6	2	11.8	3	6.4
	Other	35	16.4	9	12.7	4	23.5	5	10.6
	My child is not school aged	64	30	9	12.7	3	17.6	14	29.8
	No answer	11	5.2	8	11.3	5	29.4	10	21.3
Level of intellectual disability	Mild	71	33.3	27	38	9	52.9	21	44.7
	Moderate	117	54.9	35	49.3	2	11.8	16	34
	Severe	19	8.9	3	4.2	0	-	0	-
	No response	6	2.8	6	8.5	6	35.3	10	21.3
Additional therapies received *individuals gave multiple responses	Speech	134	62.9	53	74.6	9	52.9	28	59.6
	Occupational	99	46.5	47	66.2	6	35.3	22	46.8
	Life skills	53	24.9	5	7	2	11.8	3	6.4
	Physical	50	23.5	30	42.3	4	23.5	18	38.3
	Social	30	14.1	12	16.9	2	11.8	5	10.6
	Other	22	10.3	13	18.3	2	11.8	7	14.9
	No response	41	19.2	8	11.3	5	29.4	13	27.7
Sex	Male	117	54.9	36	50.7	9	52.9	17	36.1
	Female	91	42.7	30	42.3	3	17.6	20	42.6
	No response	5	2.3	5	7	5	29.4	10	21.3
Additional medications	Yes	138	64.8	40	56.3	10	58.8	17	36.2
	No	72	33.8	26	36.6	2	11.8	21	44.7
	No response	3	1.4	5	7	5	29.4	9	19.1
Current age	Less than 12 months	0	-	0	-	0	-	1	2.1
	1 year- 10 years	71	33.3	43	60.6	7	41.2	26	55.3
	11 years-20 years	68	31.9	16	22.5	4	23.5	9	19.1
	21 years- 30 years	34	16	2	2.8	1,	5.9	2	4.3
	31 years- 40 years	25	11.7	2	2.8	0	-	0	-
	41 years- 50 years	7	3.3	2	2.8	0	-	0	-
	51 years – 60 years	4	1.9	0	-	0	-	0	-
	61 years- 70 years	1	0.5	0	-	0	-	0	-
	No response	3	1.4	6	8.5	5	29.4	9	19.1
Age at start of administration	Less than 12 months	-	-	-	-	3	17.6	6	12.8
	1 year – 10 years	-	-	-	-	5	29.4	25	53.2
	11 years – 20 years	-	-	-	-	4	23.5	8	17
	21 years – 30 years	-	-	-	-	1	5.9	2	4.3
	31 years – 40 years	-	-	-	-	0	-	0	-
	No response					4	23.5	6	12.8

Figure 1.

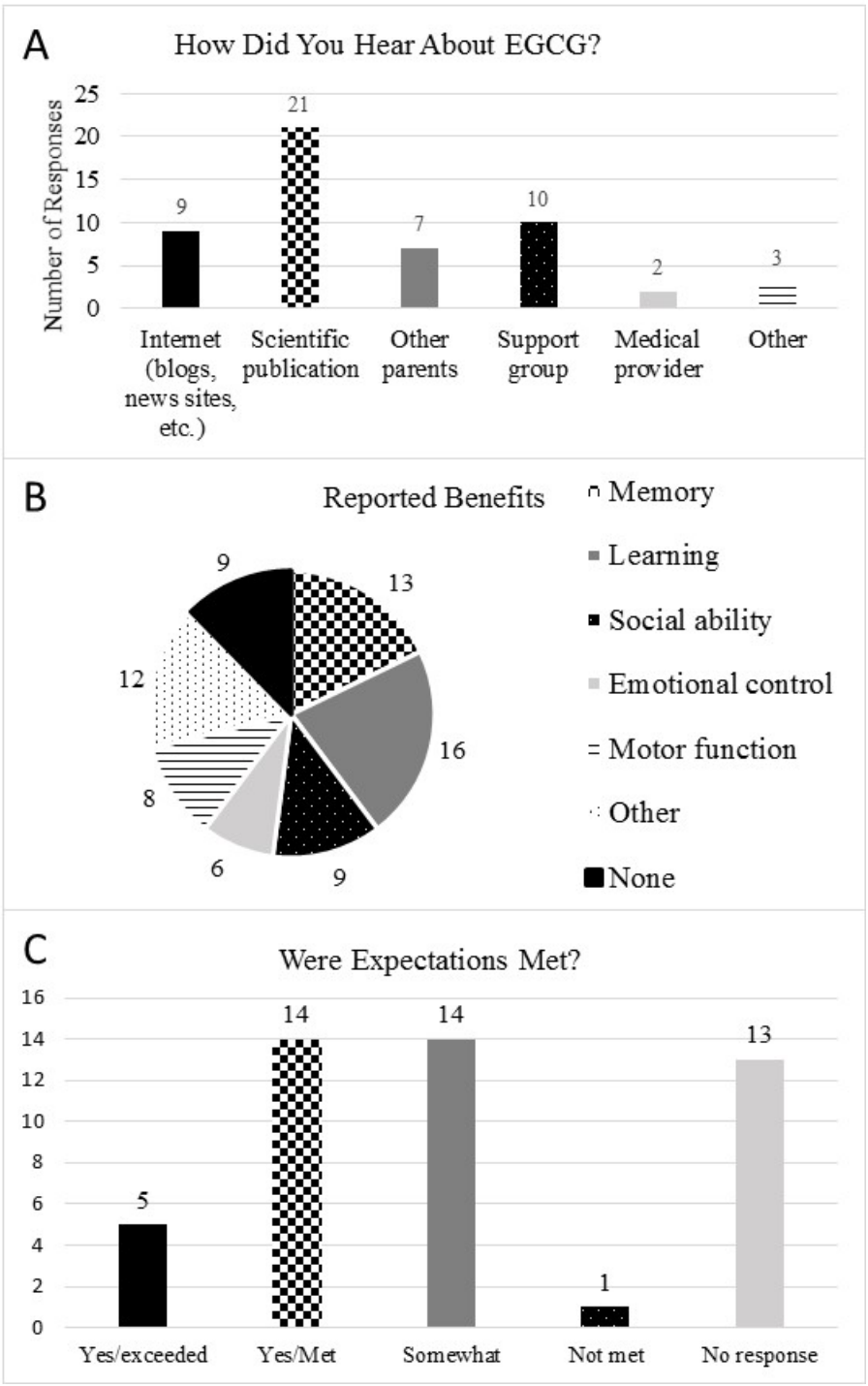
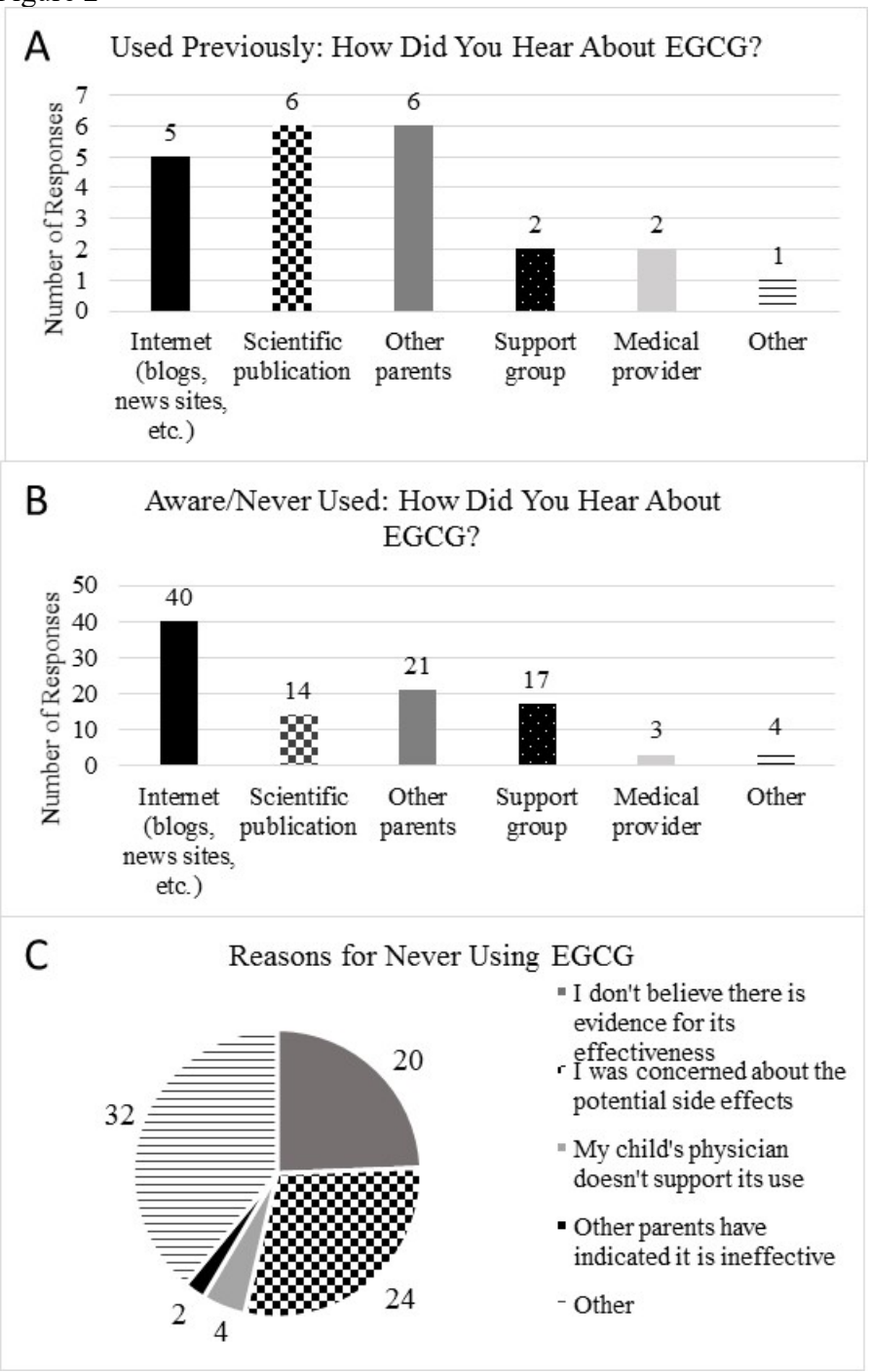

A
How Did You Hear About EGCG?
Number of Responses
25
20
15
10
5
0
9
21
7
10
2
3
Internet (blogs, news sites, etc.)
Scientific publication
Other parents
Support group
Medical provider
Other
B
Reported Benefits
9
13
16
9
6
8
12
Memory
Learning
Social ability
Emotional control
Motor function
Other
None
C
Were Expectations Met?
16
14
12
10
8
6
4
2
0
5
14
14
1
13
Yes/exceeded
Yes/Met
Somewhat
Not met
No response

Figure 2


A
Used Previously: How Did You Hear About EGCG?
Number of Responses
0
1
2
3
4
5
6
7
5
6
6
2
2
1
Internet (blogs, news sites, etc.)
Scientific publication
Other parents
Support group
Medical provider
Other
B
Aware/Never Used: How Did You Hear About EGCG?
Number of Responses
0
10
20
30
40
50
40
14
21
17
3
4
Internet (blogs, news sites, etc.)
Scientific publication
Other parents
Support group
Medical provider
Other
C
Reasons for Never Using EGCG
20
24
4
2
32
I don't believe there is evidence for its effectiveness
I was concerned about the potential side effects
My child's physician doesn't support its use
Other parents have indicated it is ineffective
Other

Supplemental Table 1: Commonly reported green tea extracts

Commonly Reported Green Tea Extracts				
Name	Number of reported users (prior and current)	Polyphenol content	Cost per capsule/mL	Average reported mg/day
Nutrivene*	9	*See below	NA	9.5
Nutrivene D	1	Does not contain EGCG	$0.28	NA
Nutrivene polyphenol support	4	98% polyphenols (588mgs) and 45% EGCG (270mgs) per serving	$0.50	19.3
Swanson,Äôs Ultra GreenSelect Green Tea Phytosome	6	19-25% polyphenols (114-150mgs), 13% EGCG (78mgs)	$0.28	255
Now Foods EGCG Green tea extract	6	200mg EGCG (50%), 80% catechins	$0.17	260
Life Extension Mega Green Tea Extract (Decaf)	4	98% polyphenols (45% EGCG- 326.25mgs)	$0.23	712.5
Teavigo	3	94% EGCG (141mg) per 1 capsule	$0.22	217
Vitacost Green Tea Select	2	250mg EGCG (50%), 98% polyphenols (490 mgs), 80% catechins (400mgs)	$0.6	150
Elite Green Tea Phytosomal Extract	2	13mg EGCG (40%), 20mg polyphenols (60%)	$0.18	200
Life Extension Megan Green Tea Extract (Caffeinated)	1	98% polyphenols (45% EGCG- 326.25mgs)	$0.23	200
Solaray Double Strength Green Tea Capsules	1	250mg EGCG (50%), 98% polyphenols (490 mgs), 80% catechins (400mgs)	$0.28	500
Nature’s Answer Super Green Tea	1	100mg GTE: EGCG (50%), 95% polyphenols, 80% catechins	$0.24	NR
Relentless Improvement Decaffeinated EGCG	1	670mg EGCG per capsule for 1340mg per serving, more than 60% EGCG. Polyphenols standardized to 98%+.	$0.30	409
Average			$0.25	267
Others reported: Kenko Organic Matcha Green Tea powder, Organic Matcha culinary grade green tea powder, “drink green tea”, Trader Joe’s Decaf Green Tea, Encha organic powder, “different supplements which were laboratory tested for their biological activity”, matcha powder *Indicates respondent only reported brand				